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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/487,032	06/07/95	SMITH D	GTN-001

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EXAMINER	
PORTNER, V	
ART UNIT	**PAPER NUMBER**
1645	32

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant
08/487,032	Smith et al
Examiner	**Group Art Unit**
Portner	1645

☒ Responsive to communication(s) filed on *Oct 30, 2000*.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *113-120, 123-125, 127-135, 149, 150, and 196-224* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *113-120, 123-125, 127-135, 149, 150, and 196-224* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claims 113-120, 123-125,127-135,149-150,196-213 and new claims 214-224 are pending.

Rejections Withdrawn

1. Claims 120-123,132-135, 149,152, 155 rejected under 35 U.S.C. 102(b) as being anticipated by Newman et al.

Rejections Maintained

2. Claims 113-120, 123-125,127-135,149-150,196-213 and 214-224 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial, a credible asserted utility or a well established utility.

3. Claims 113-120, 123-125,127-135,149-150,196-213 and 214-224 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

4. Claims 113-120, 123, 132-133,149,196-201,204,205-212,214-219, 220-224 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the

specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record on paper number 26.

Response to Arguments

5. Applicant's arguments filed October 30, 2000 have been fully considered but they are not persuasive.

6. The rejection of claims 113-120, 123-125,127-135,149-150,196-213 and 214-224 under 35 U.S.C. 101 is argued by Applicant:

> The present invention features a novel surface protein from the bacteria Helicobacter pylori. Applicant has described the chemical, physical and biological properties of the polypeptide set forth as SEQ ID NO 764. Applicant asserts that the polypeptides of the invention can be used for diagnostic and therapeutic purposes with regard to H.pylori infection; for generating antibodies; and to evaluate compounds useful as activators or inhibitors of the bacterial life cycle.

it is further asserted:

> 'the polypeptide set forth as SEQ ID No 764 is a surface protein of the H.pylori pathogen, and, as such, is an attractive target for intervention.'

7. Upon consideration of Applicant's arguments that the invention is :

a."the amino acid sequence of SEQ ID NO 764 (page 5, paragraph 2, lines 1-2);

b.the polypeptide "is an attractive target for intervention"(page 5, paragraph 4, lines 2-3);

c.the utilities are defined as "proposed utilities of the claimed polypeptides" (page 5, paragraph 5, line 1);

d.arguments based upon publications after the filing date of the instant Application which characterize proteins that 'correspond substantially' to SEQ ID NO 764:(page 6, paragraph 1, lines 10-11), the examiner has taken the position that the claimed invention is not limited to SEQ ID No 764, but is drawn to polypeptides that share as few as 10 amino acids of SEQ ID NO 764, a sequence of 170 amino acids. The claimed invention may comprise 10, 20, 50 or 100 amino acids selected from SEQ ID NO 764 consecutively or non-consecutively. The resulting polypeptide need not look anything like SEQ ID NO 764, especially when it only shares as little as 6 % of the over all sequence of SEQ ID No 764 (10 of 170 amino acids).

A representative number of species for the claimed genus of polypeptides ~~have~~ has not been described, nor ~~have they been~~ enabled as diagnostic or vaccine polypeptides. Just because a polypeptide is defined as a surface polypeptide, does not automatically define the polypeptide as a diagnostic or vaccine antigen.

Even if the claimed invention were limited to just SEQ ID NO 764, the asserted biological activity of a polypeptide molecule is not defined by a linear sequence of amino acids. While a SEQ ID NO provides insight into the overall molecular structure, and the physical characteristics of the individual components, the SEQ ID NO does not define biological activity of the three dimensional polypeptide molecule in the native context. The biological activity of SEQ ID NO 764 has not been described in the instant Specification.

The cited references, Doig et al (1995) and Bains et al (2000), supplied by Applicant, compare SEQ ID NO 764 to the protein of Bains et al, which has been 'shown to be antigenic in vivo with both patient sera and specific monoclonal antibodies'. It is clear to the examiner that the antigen of Bains induces antibodies, these antibodies are present in patients that are still sick. The antibodies induced in vivo are not protective antibodies because infection persists. The protein of Bains has 250 amino acids and functions as a porin. The claimed polypeptide of SEQ ID No 740 only has 170 amino acids and no credible asserted utility. The protein of Bains is not defined as the same polypeptide as the instantly claimed invention, but is argued to 'correspond substantially'. The instant specification does not define SEQ ID No 764 as corresponding substantially to the porin of Bains. ~~What~~ the meaning of the phrase 'corresponds substantially' ~~means~~ with respect to SEQ ID No 764, has not been defined the instant specification.

The polypeptide of the invention is argued to be immunogenic and could induce antibodies which in turn could be used to identify the polypeptide, how circular reasoning defines a substantial, credible or well established utility has not been established.

8. Applicant urges, due to homology between P2 protein and the claimed polypeptides of SEQ ID NO 764, the polypeptides of SEQ ID NO 764 would have shared characteristics, and biological activity and thus would have diagnostic and vaccine utility.

9. It is the position of the examiner that the disease conditions caused by H.pylori and Haemophilus influenza are very different. The virulence factors associated with each of these

pathogens also differ. The regions of the body that each pathogen infects and causes disease are not the same.

Comparison of SEQ ID NO 764 with Haemophilus influenza P2 porin, does not define SEQ ID No 764 as having the same biological characteristics as the claimed polypeptides. H.pylori vaccines are not predictable. Monath, Heap and Dunkley all show the induction of significant immune responses to H.pylori antigens without the induction of an immune response that protects against infection.

Comparison of SEQ ID NO 764 with Haemophilus influenzae porin protein P2 (US Pat. 6,153,406) shows SEQ ID NO 764 (170 amino acids) shares **43 amino acids** with SEQ ID NO 10 (342 amino acids) of Tai et al (see attached alignment) .

Comparison of SEQ ID NO 764 with H.pylori multimeric urease (US Pat.5,837,240) shows SEQ ID No 764 (170 amino acids) shares **40 amino acids** with the overall sequence of SEQ ID No 12 (518 amino acids) of Lee (see attached alignment) .

Comparison of SEQ ID NO 764 with EG III cellulase (US Pat. 5,475,101) from Trichoderma longibrachiatum shows that SEQ ID NO 764 (170 amino acids) shares **35 amino acids** with SEQ ID NO 13(221 amino acids) of Ward et al (see attached alignment) .

Comparisons made based upon sequence alignment of SEQ ID NO 764 with microbial proteins known in the art does not define the biological activity of SEQ ID NO 764 as that of the proteins that have shared homology. The sequence alignments show homology between three

very different proteins of different lengths and different functionalities. The cellulase of Ward shows ~~that~~ the greatest over all sequence similarity relative to the size of the full length polypeptide.

10. Argument is made that no evidence has been made of record that questions the asserted utilities for SEQ ID No 764:

> ' No evidence has been made of record that Applicant's assertions regarding utilities of the claimed polypeptides as diagnostic and/or therapeutic agents for H.pylori would not be considered credible to one of skill in the art.(page 6, paragraph 2, lines 5-7)'.

11. Upon consideration of the arguments and the references submitted by Applicant, the examiner believes that evidence has been made of record that defines portions of SEQ ID NO 764 to evidence antigenic cross reactivity with the P2 porin of Haemophilus pathogen . The existence of cross reactive epitopes would induce cross reactive antibodies which would result in a false positive diagnostic result. Therefore, Applicant has made of record arguments and evidence that polypeptides of SEQ ID No 764 would not serve as a diagnostic polypeptide for H.pylori infection due to the existence of conserved portions of SEQ ID NO 764 being shared with H.influenzae, both are human pathogens.

With respect to arguments made regarding evidence to show that SEQ ID No 764 is not a vaccine antigen, the examiner would like to point out the fact that Rappouli et al (1993) and HP World Wide (1991) documents have previously been made of record which show that H.pylori

vaccines are in the developmental stages and are not predictable. HP World Wide cites Dunkley and Heap who found H.pylori compositions did not induce protective immunity. No showing has been made of record that indicates that the conserved portions of the H.influenza P2 porin are those portions responsible for the induction of protective immune response against H.influenza, and that these conserved portions would also induce a protective immune response against Helicobacter pylori as well. Therefore, arguments that H.influenza P2 protein and Helicobacter polypeptide SEQ ID No 764 are both protective antigens are not convincing.

The rejection made of record under 35 U.S.C. 101, is maintained and the enablement rejection is maintained as well, for the same reasons made of record and responses above with respect to the lack of utility of the claimed polypeptide.

12. The rejection of claims 113-120, 123, 132-133, 149, 196-201 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is argued (see page 15, paper number 28, paragraph 3) through asserting that there is adequate description of the claimed invention:

> 'the claimed genus of polypeptides having at least 60% sequence identity with SEQ ID NO: 764 and polypeptides encoded by a nucleic acid sequence which hybridizes under high stringency conditions to the complement of a nucleotide sequence encoding SEQ ID NO 764 is

identified by structural features that are described in the specification, recited in the claims, and commonly possessed by its members.'

13. In response to Applicant's assertion, it is the position of the examiner that while the instant specification suggests polypeptides of the recited structural components held in common with SEQ ID NO 764, no structural polypeptides of the same functional characteristics of SEQ ID NO 764 have been described. The examiner has not made a New Matter rejection, but made a lack of written description for the claimed genus of polypeptides.

Applicant quotes the interim guidelines and focuses on the structure of the claimed polypeptide as the relevant identifying characteristic. The Interim Guidelines emphasizes the importance of disclosing relevant identifying characteristics.

As discussed under paragraphs 7 and 9 above, the only physical characteristic disclosed is the amino acid sequence, the only structural characteristic disclosed is the amino acid sequence and the only chemical characteristic disclosed is that presented by the amino acid sequence. Only the SEQ ID NO is disclosed to describe the invention. A representative number of polypeptides that differ from SEQ ID No 764, and would also evidence the same or equivalent biological function do not evidence original descriptive support.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived.

See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Similarly, applicants have not disclosed any information which is 3' and 5' to the polynucleotide sequence of SEQ ID NO:764 and therefore clearly lacks written description for the broad class of polynucleotides encoding SEQ ID NO:764. In the instant case, the specification provides only written description for a polypeptide that is encoded by a polynucleotide consisting of SEQ ID NO:764. No variant polypeptides have been described in such a way to reasonably convey to one skilled in the relavant art that Applicant had possession of the claimed invention.

For arguments sake, assume that the gene that encodes the full length Helicobacter pylori protein that comprises the now claimed polypeptide is within the scope of the claimed invention based upon the claim language recited. The claimed invention, SEQ ID NO 764, has not been described as the full length coding region of a protein, but an isolated polypeptide that comprises SEQ ID NO 764 would read on a full length protein, which would be encoded by the gene for the protein. As the term polypeptide encompasses proteins, the scope of the claimed invention encompasses the full length protein that comprises SEQ ID NO 764. Helicobacter polypeptides (proteins) that are larger than 170 amino acids and comprise SEQ ID NO 764 lack original descriptive support in the instant specification.

14. At page 15, paragraph 4, of paper number 28, Amendment G, it is argued that the claim limitations of claims 113 and 120 are drawn to isolated polypeptides which include **an amino acid** sequence that is identical to a naturally occurring H.pylori peptide.

15. The examiner understands that the claimed polypeptide contains an amino acid sequence of a naturally occurring H.pylori polypeptide, but how large a portion of a naturally occurring polypeptide the claimed isolated polypeptide contains, is not recited in claim 113, thus any size amino acid sequence is being claimed.

While claim 120 requires the isolated polypeptide to be at least 10 amino acid residues in length, the amino acid sequence need not be identical to SEQ ID NO 764, but must only be encoded by a nucleic acid sequence that will hybridize to the complement of SEQ ID NO 764. The nucleic acid sequence could share 60-70 % homology and still hybridize to SEQ ID NO 764.

What the sequence of the isolated polypeptide is with the recited characteristics defined in claims 113 and 120, other than the disclosed SEQ ID No 764, does not evidence original descriptive support. A single disclosed species does not provide original descriptive support and show possession for the now claimed genus of polypeptides.

With respect to the claimed polypeptides of claims 125-131,134-135 , it is the position of the examiner that the claim is described for Helicobacter polypeptides up to 170 amino acids that are encoded by SEQ ID No 764. Helicobacter polypeptides larger that 170 amino acids and comprise SEQ ID NO 764 do not evidence original descriptive support. As no upper limit is recited in the claim, Helicobacter pylori polypeptides greater than 170 amino acids are

encompassed by the claim language which do not meet the requirement for written description.

For example, Applicant submitted Bains et al (publishded in year 2000) as 'substantially corresponding' to the claimed invention. The protein (a type of polypeptide), of Bains, comprises 250 amino acids and comprises at least 10,20,50 and 100 amino acids of a naturally occurring Helicobacter polypeptide. The protein of Bains is not described in the instant specification, the document was published in year 2000, therefore, even though there is substantial correspondence of the claimed invention to the polypeptide of Bains, original descriptive support for polypeptides that comprise SEQ ID No 764 and are larger than the 170 amino acids of Seq ID NO 764 do not meet the written description requirement under 35 USC 112, first paragraph.

Conclusion

16. No claims are allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

19.Doig et al (October 1994) is cited to show a Helicobacter pylori porin of 31 kDa (page 4531, col. 2, last paragraph).

20.Tufano et al (April 1994) is cited to show a Helicobacter pylori porin of 31 kDa.

21.Tai et al (6,153,406) is cited to show Haemophilus influenzae P2 porin.

22.Lee et al (5,837,240) is cited to show multimeric urease of Helicobacter pylori.

23.Ward et al (5,475,101) is cited to show endoglucanase III cellulase of Trichoderma longirachiatum.

24.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp

January 24, 2000

L. F. Smith

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